Fas ligand (FasL), results in apoptosis of the hepatocyte. The second method, which involves granzyme and perforin, also results in apoptosis of the hepatocyte.

e. Hepatitis C, chronic inflammation, and liver cancer

Chronic inflammation is an unfortunate naturally occurring adverse event that can occur during immune response against hepatitis C. This chronic inflammation often results in cirrhosis of the liver as well as liver cancer, that is, hepatocellular carcinoma (HCC). The damage that is caused by the immune system to the liver is separate from, and in addition to, that caused by the virus alone (40,41,42,43). Hence, chronic HCV infection can be classified as a disorder of chronic inflammation.

f. Dendritic cells

Dendritic cells (DCs) are antigen-presenting cells (APCs) that process antigens, and present them to T cells. Dendritic cells also secrete various cytokines, including interleukin-12 (IL-12) and IFN-alpha. Dendritic cells occur in two lineages, the *myeloid DCs* and the *plasmacytoid DCs*. The myeloid DCs secrete IL-12, which provokes Th1-type immune response against hepatocytes infected by the HCV. The plasmacytoid DCs secrete interferon-gamma (IFN-gamma), a cytokine having a direct inhibitory effect on hepatitis C viruses. Immune response against HCV involves both types of dendritic cells (44).

g. Sources of interferons during HCV infections

Interferon-alpha (IFN-alpha) and interferon-gamma (IFN-gamma), both naturally expressed and administered as a drug, are issues in HCV infections. Therapeutic IFN-gamma, which is not part of the standard of care for HCV, has been tested for potential therapeutic effects, as shown by Balan et al. (45) and Shin et al. (46).

[40] Cruise MW, Lukens JR, Nguyen AP, Lassen MG, Waggoner SN, Hahn YS. Fas ligand is responsible for CXCR3 chemokine induction in CD4+ T cell-dependent liver damage. *J Immunol*. 2006;176:6235–6244.

[41] Cruise MW, Melief HM, Lukens J, Soguero C, Hahn YS. Increased Fas ligand expression of CD4+ T cells by HCV core induces T cell-dependent hepatic inflammation. *J Leukoc Biol*. 2005;78:412–425.

[42] Urbani S, Amadei B, Fisicaro P, et al. Heterologous T cell immunity in severe hepatitis C virus infection. *J Exp Med*. 2005;201:675–680.

[43] Bertoletti A, Maini MK. Protection or damage: a dual role for the virus-specific cytotoxic T lymphocyte response in hepatitis B and C infection? *Curr Opin Immunol*. 2000;12:403–408.

[44] Kanto T, Hayashi N. Immunopathogenesis of hepatitis C virus infection: multifaceted strategies subverting innate and adaptive immunity. *Intern Med*. 2006;45:183–191.

[45] Balan V, Rosati MJ, Anderson MH, Rakela J. Successful treatment with novel triple drug combination consisting of interferon-gamma, interferon alfacon-1, and ribavirin in a nonresponder HCV patient to pegylated interferon therapy. *Dig Dis Sci*. 2006;51:956–959.

[46] Shin EC, Protzer U, Untergasser A, et al. Liver-directed gamma interferon gene delivery in chronic hepatitis C. *J Virol*. 2005 November;79:13412–13420.